## REMARKS

Claims 1-8, 10-17, 23, 24, and 31-50 were pending. Claims 18-21 and 25-30 were withdrawn by the examiner as being drawn to a non-elected invention. Claims 31, 32, 36-37, 44, 49, and 50 are amended herein. New claims 51-65 are added. Support for the amendments and new claims is found throughout the specification, and thus it is believed that no new matter has been added. Claims 1-8, 10-30, 33-35, 38-43, and 45-48 are cancelled. Claims 31, 32, 36, 37, 44 and 49-65 are pending. No claim is allowed.

Applicants gratefully acknowledge the entry of the request for continued examination and entry of the amendment filed on July 6, 2004 as well as the withdrawal of outstanding claim rejections under 35 U.S.C. § 112, first paragraph and 35 U.S.C. § 102 (b). Applicants also acknowledge the priority grant to the cited provisional applications.

**Objection to the Specification**

The amendment to the specification filed July 22, 2003 is objected to under 35 U.S.C. § 132 as it allegedly introduces new matter. According to the examiner, while SEQ ID NOs:1-4 are expressly disclosed, they are not expressly disclosed as encoding (or being) the enzyme BD1911 or BD1912. Applicants traverse this rejection.

Applicants maintain that defining the disclosed enzymes as being the specific sequences disclosed is not new matter in view of the express disclosure of the sequences as well as the enzymes and their functional activities. No new matter has been added in making the identification of the enzymes explicit in the specification. Nonetheless, in an effort to expedite prosecution of this application, Applicants have amended the specification to delete this reference, rendering the objection moot.

In view of the above, Applicants respectfully request the withdrawal of the rejection to the specification.

**Objections to the Claims**

Claim 1 is objected to for improper punctuation. According to the Examiner, no comma is required after SEQ ID NO:2 since only two items are listed. Claim 1 is cancelled herein, rendering the above objection moot.

Claim 23 is objected to under 37 C.F.R. § 1.75 (c) as allegedly being of improper dependent form for failing to further limit the subject matter of the previous claim. According to the Examiner, the limitation defining the sequence that encodes SEQ ID NOs:2 or 4 do not further limit claim 1 because it does not change the nature of SEQ ID NOs: 2 or 4. Applicants traverse this objection. Claim 23 is cancelled herein, rendering the rejection moot.

In view of the above, Applicants respectfully submit that the basis for the rejection may be withdrawn.

**Rejection Under 35 U.S.C. § 112, second paragraph**

Claims 1-8, 10, 23, 24, 38-43, 45-46, and 49-50 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. According to the Examiner, the phrase "reaction components" is unclear. Claims 44 and 50 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite in its use of the limitation "the same enzymatic activity as nucleic acid sequence from which it varies." The Examiner alleges the activity being defined is that of a polypeptide, which does not have the activity of a nucleic acid sequence. Applicants traverse these rejections.

Claims 1 and 24 are canceled herein, rendering the rejection regarding "reaction components" moot.

Claim 44 is amended herein to indicate that the same enzymatic activity of the claim is from the polypeptide encoded by the claimed nucleic acid sequence, rendering the above rejection moot.

Accordingly, the basis for the rejection may be removed.

**Rejection Under 35 U.S.C. § 112, first paragraph - Enablement**

Claims 1-8, 10-17, 23, 24, 33, 38-43, and 45-48 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement. According to the

Examiner, methods of producing enantiomerically pure α-substituted carboxylic acid would require undue experimentation. Claims 31-32, 34-37, 44, 49, and 50 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement for methods producing any α-substituted carboxylic acid. According to the Examiner, the breadth of the claims is virtually boundless using any aldehyde or ketone. The Examiner asserts that nitrilases are somewhat promiscuous enzymes in their substrate specificity and have limitations to their selectivity. Claims 24, 38-44, 46, 48, and 50 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement for sequences related to SEQ ID NOs: 2 and 4 with as little as 70% identity. The Examiner notes that the prior art is relatively silent on the generic structure of nitrilases and that the instant specification lacks any description that provides the residues important to the nitrilase nature of the molecule. Applicants traverse these rejections.

Applicants respectfully submit that specification provides reasonable enablement for the production of enantiomerically pure α-substituted carboxylic acids using nitrilases of the claimed methods. Nonetheless, in an effort to expedite prosecution, the claims are canceled herein.

The specification also provides reasonable enablement for the use of the claimed nitrilases to produce an α-substituted carboxylic acid. Nitrilases are a class of enzymes defined by a specific reaction - the hydrolysis of a non-peptide carbon-nitrogen bond. This is a known and well characterized chemical reaction that is routinely practiced in the art. Moreover, nitrilase substrates are easily identified and Dr. DeSantis attests to the routine nature of determining substrate specificity of the nitrilase enzymes in the declaration provided. *See* Exhibit A at ¶¶2-4. Thus, the breadth of the claimed methods is entirely appropriate and requires only routine experimentation to fully use. The cited Robertson article provides further support for the routine nature of determining nitrilase substrates. All of the 137 nitrilases identified displayed enzymatic activity for two prototypical nitrile substrates. *See* Robertson at 2430. The instant claims are drawn to two disclosed nitrilase enzymes and a related subgenus with a particular substrate reactivity. The identification of a nitrilase by activity using an aldehyde or ketone substrate is easily accomplished and sufficiently predictable using the guidance provided in the specification and what is known in the art.

Applicants further submit that the specification provides reasonable enablement for the genus of nucleic acids of the claimed methods. The specification describes the genus used in the methods by characteristics or properties that include, but are not limited to the functionality of the encoded protein. More specifically, the specification describes the genus in terms of structure (the exemplary nucleic acids SEQ ID NO:2 or SEQ ID NO:4) and physio-chemical properties (*e.g.*, percent sequence identity) in addition to function (*e.g.*, encoding polypeptides having nitrilase activity). Applicants respectfully submit that describing a genus of polynucleotides in terms of structure (*e.g.*, exemplary sequence), physio-chemical properties (*e.g.*, % sequence identity) and function satisfies the written description requirement of § 112, first paragraph.

The guidelines provides by the Office recognize the sufficiency of such disclosure for the purposes of the written description requirement. Example 14 of the Guidelines concluded that a claim reciting variants claimed by sequence identity to a sequence (specifically, "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B) satisfies the written description requirement of section 112, first paragraph. The USPTO guidelines recognize that the written description requirement is met for a genus of polynucleotides described by structure (*e.g.*, an exemplary sequence), a physio-chemical property (*e.g.*, a % sequence identity or stringent hybridization) and a defined function. Applicants respectfully aver that these guidelines apply to the claimed invention, *i.e.*, they recognize that claims directed to a genus of polynucleotides described by an exemplary sequence, a % sequence identity (*e.g.*, at least 70%, 80%, 90% or more sequence identity) and a defined function (*e.g.*, nitrilase activity) meet the written description requirement. *Additional* specific structural characteristics or elements are not required.

Finally, Applicants note that the specification provides sufficient guidance to identify sequences with at least 70% sequence identity that retain the functional activity of the claimed enzyme. For example, suitable conservative substitutions, insertions, and deletions are described at page 11, lines 1-18. Methods to determine the functional activity are routine in the art with all of the necessary components readily available. Working examples for functional activity are provided and the sequence at issue disclosed, thus undue experimentation is not required.

Accordingly, the basis for these rejections may be withdrawn.

## CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding objections and rejections of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 564462006600.

Respectfully submitted,

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By: _____

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